

## CLAIMS:

1. A peptide having a sequence of amino acids which is identical to a sequence of consecutive amino acids found within amino acids 695 to 698 (SEQ ID NO. 10) of the human blood clotting factor Va.  
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2. The peptide of claim 1 wherein the peptide exhibits an  $IC_{50}$  of less than about 100  $\mu M$ , the  $IC_{50}$  being the amount of the peptide that inhibits 50% of the activity of human factor Va.  
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3. The peptide of claim 2 wherein the peptide exhibits an  $IC_{50}$  of less than about 15  $\mu M$ .
4. The peptide of claim 3 wherein the peptide exhibits an  $IC_{50}$  of about 1.6  $\mu M$ .  
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5. The peptide of claim 4 wherein the peptide exhibits an  $IC_{50}$  of about 500 nM.
6. The peptide of claim 1 wherein the peptide exhibits the amino acid sequence DYDY.  
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7. The peptide of claim 1 wherein the peptide exhibits the amino acid sequence DYDYQ.  
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8. A pharmaceutical composition comprising the peptide of claim 1.
9. A method for treating human subjects having blood clotting disorders, the method comprising administering the pharmaceutical composition of claim 8 to the human subjects.  
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10. A peptide analogue that mimics the peptide of claim 1.

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11. A peptide comprising a sequence of amino acids which is identical to a sequence of consecutive amino acids found within amino acids 695 to 699 (SEQ ID NO. 11) of the human blood clotting factor Va.

5 12. The peptide of claim 11 wherein the peptide exhibits an  $IC_{50}$  of less than about 100  $\mu M$ , the  $IC_{50}$  being the amount of the peptide that inhibits 50% of the activity of human factor Va.

10 13. The peptide of claim 12 wherein the peptide exhibits an  $IC_{50}$  of less than about 15  $\mu M$ .

14. The peptide of claim 13 wherein the peptide exhibits an  $IC_{50}$  of about 1.6  $\mu M$ .

15 15. The peptide of claim 14 wherein the peptide exhibits an  $IC_{50}$  of about 500 nM.

16. The peptide of claim 11 wherein the peptide exhibits the amino acid sequence DYDY.

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17. The peptide of claim 11 wherein the peptide exhibits the amino acid sequence DYDYQ.

18. A pharmaceutical composition comprising the peptide of claim 25 11.

19. A method for treating human subjects having blood clotting disorders, the method comprising administering the pharmaceutical composition of claim 18 to the human subjects.

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20. A peptide analogue that mimics the peptide of claim 11.

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21. A peptide adapted to inhibit blood coagulation by inhibiting thrombin generation, the peptide comprising an amino acid sequence DYDY wherein one of the Y amino acids is sulfonated (SEQ ID NO. 12, 13).

5        22. The peptide of claim 21 wherein the amino acid sequence is DY(-SO<sub>3</sub>)DY.

23. The peptide of claim 21 wherein the amino acid sequence is DYDY(-SO<sub>3</sub>).

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24. A pharmaceutical composition comprising the peptide of claim 21.

15        25. A method for treating human subjects having blood clotting disorders, the method comprising administering the pharmaceutical composition of claim 24 to human subjects.

26. A peptide analogue that mimics the peptide of claim 21.

20        27. A peptide adapted to inhibit blood coagulation by inhibiting thrombin generation, the peptide comprising an amino acid sequence DYDY wherein both of the Y amino acids are sulfonated (SEQ ID NO. 14).

25        28. The peptide of claim 27 wherein the amino acid sequence is DY(-SO<sub>3</sub>)DY(-SO<sub>3</sub>).

29. A pharmaceutical composition comprising the peptide of claim 27.

30        30. A method for treating human subjects having blood clotting disorders, the method comprising administering the pharmaceutical composition of claim 29 to human subjects.

31. A peptide analogue that mimics the peptide of claim 27.

32. A peptide adapted to inhibit blood coagulation by inhibiting thrombin generation, the peptide comprising an amino acid sequence DYDYQ wherein one of the Y amino acids is sulfonated (SEQ ID NO. 7, 8).

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33. The peptide of claim 32 wherein the amino acid sequence is DY(-SO<sub>3</sub>)DYQ.

34. The peptide of claim 32 wherein the amino acid sequence is  
10 DYDY(-SO<sub>3</sub>)Q.

35. A pharmaceutical composition comprising the peptide of claim 32.

15 36. A method for treating human subjects having blood clotting disorders, the method comprising administering the pharmaceutical composition of claim 35 to human subjects.

20 37. A peptide analogue that mimics the peptide of claim 32.

38. A peptide adapted to inhibit blood coagulation by inhibiting thrombin generation, the peptide comprising an amino acid sequence DYDYQ wherein both of the Y amino acids are sulfonated (SEQ ID NO. 9).

25 39. The peptide of claim 38 wherein the amino acid sequence is DY(-SO<sub>3</sub>)DY(-SO<sub>3</sub>)Q.

40. A pharmaceutical composition comprising the peptide of claim 38.

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41. A method for treating human subjects having blood clotting disorders, the method comprising administering the pharmaceutical composition of claim 40 to human subjects.

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42. A peptide analogue that mimics the peptide of claim 38.

43. A pharmaceutical composition adapted for inhibiting thrombin generation, the composition comprising a peptide including an amino acid  
5 sequence DYDY (SEQ ID NO. 10).

44. The pharmaceutical composition of claim 43 further comprising a carrier.

10 45. The pharmaceutical composition of claim 43 wherein one of the Y amino acids of the amino acid sequence is sulfonated.

46. The pharmaceutical composition of claim 45 wherein the amino acid sequence of the peptide is DY(-SO<sub>3</sub>)DY.

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47. The pharmaceutical composition of claim 45 wherein the amino acid sequence of the peptide is DYDY(-SO<sub>3</sub>).

20 48. The pharmaceutical composition of claim 43 wherein both of the Y amino acids of the amino acid sequence are sulfonated.

49. The pharmaceutical composition of claim 48 wherein the amino acid sequence of the peptide is DY(-SO<sub>3</sub>)DY(-SO<sub>3</sub>).

25 50. A method for treating patients having blood clotting disorders, the method comprising administering the pharmaceutical composition of claim 43 to the patients.

30 51. A pharmaceutical composition comprising a peptide analogue that mimics the peptide of the composition of claim 43.

52. A pharmaceutical composition adapted for inhibiting thrombin generation, the composition comprising a peptide including an amino acid sequence DYDYQ (SEQ ID NO. 11).

53. The pharmaceutical composition of claim 52 further comprising a carrier.

5 54. The pharmaceutical composition of claim 52 wherein one of the Y amino acids of the amino acid sequence is sulfonated.

55. The pharmaceutical composition of claim 54 wherein the amino acid sequence of the peptide is DY(-SO<sub>3</sub>)DYQ.

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56. The pharmaceutical composition of claim 54 wherein the amino acid sequence of the peptide is DYDY(-SO<sub>3</sub>)Q.

57. The pharmaceutical composition of claim 52 wherein both of the  
15 Y amino acids of the amino acid sequence are sulfonated.

58. The pharmaceutical composition of claim 57 wherein the amino acid sequence of the peptide is DY(-SO<sub>3</sub>)DY-(SO<sub>3</sub>)Q.

20 59. A method for treating patients having blood clotting disorders, the method comprising administering the pharmaceutical composition of claim 52 to the patients.

60. A pharmaceutical composition comprising a peptide analogue  
25 that mimics the peptide of the composition of claim 52.

61. A pharmaceutical composition adapted for inhibiting thrombin generation in a human, the composition comprising a peptide including an amino acid sequence DYDY in which one of the Y amino acids is sulfonated  
30 (SEQ ID NO. 12, 13).

62. The pharmaceutical composition of claim 61 further comprising a carrier.

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63. The pharmaceutical composition of claim 61 wherein the amino acid sequence of the peptide is DY(-SO<sub>3</sub>)DY.

64. The pharmaceutical composition of claim 61 wherein the amino acid sequence of the peptide is DYDY(-SO<sub>3</sub>).

65. A method for treating human subjects having blood clotting disorders, the method comprising administering the pharmaceutical composition of claim 61 to human subjects.

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66. A pharmaceutical composition comprising a peptide analogue that mimics the peptide of the composition of claim 61.

67. A pharmaceutical composition adapted for inhibiting thrombin generation in a human, the composition comprising a peptide including an amino acid sequence DYDY in which both of the Y amino acids are sulfonated (SEQ ID NO. 14).

68. The pharmaceutical composition of claim 67 further comprising a carrier.

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69. The pharmaceutical composition of claim 67 wherein the amino acid sequence of the peptide is DY(-SO<sub>3</sub>)DY(-SO<sub>3</sub>).

70. A method for treating human subjects having blood clotting disorders, the method comprising administering the pharmaceutical composition of claim 67 to human subjects.

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71. A pharmaceutical composition adapted for inhibiting thrombin generation in a human, the composition comprising a peptide including an amino acid sequence DYDYQ, in which one of the Y amino acids is sulfonated (SEQ ID NO. 7, 8).

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72. The pharmaceutical composition of claim 71 further comprising a carrier.

73. The pharmaceutical composition of claim 71 wherein the amino acid sequence of the peptide is DY(-SO<sub>3</sub>)DYQ.

74. The pharmaceutical composition of claim 71 wherein the amino acid sequence of the peptide is DYDY(-SO<sub>3</sub>)Q.

75. A method for treating human subjects having blood clotting disorders, the method comprising administering the pharmaceutical composition of claim 71 to human subjects.

76. A pharmaceutical composition comprising a peptide analogue that mimics the peptide of the composition of claim 71.

77. A pharmaceutical composition adapted for inhibiting thrombin generation in a human, the composition comprising a peptide including an amino acid sequence DYDYQ, in which both of the Y amino acids are sulfonated (SEQ ID NO. 9).

78. The pharmaceutical composition of claim 77 further comprising a carrier.

79. The pharmaceutical composition of claim 77 wherein the amino acid sequence of the peptide is DY(-SO<sub>3</sub>)DY(-SO<sub>3</sub>)Q.

80. A method for treating human subjects having blood clotting disorders, the method comprising administering the pharmaceutical composition of claim 77 to human subjects.

81. A pharmaceutical composition comprising a peptide analogue that mimics the peptide of the composition of claim 77.



82. A method for inhibiting thrombin generation in a human patient suffering from a blood coagulation disorder, the method comprising:

administering to the patient an effective amount of a peptide that includes a sequence of consecutive amino acids found within amino acids 695 to 698 (SEQ ID NO. 10) of the human blood clotting factor Va.

83. The method of claim 82 wherein the effective amount of the peptide is in the range of from about 0.01 to 1000 mg/kg of body weight, per day.

84. The method of claim 83 wherein the effective amount of the peptide is in the range of from about 0.1 to 100 mg/kg of body weight, per day.

85. The method of claim 84 wherein the effective amount of the peptide is in the range of from about 1 to 10 mg/kg, of body weight, per day.

86. A method for inhibiting thrombin generation in a human patient suffering from a blood coagulation disorder, the method comprising:

administering to the patient an effective amount of a peptide analogue that mimics the peptide of the method of claim 82.

87. A method for inhibiting thrombin generation in a human patient suffering from a blood coagulation disorder, the method comprising:

administering to the patient an effective amount of a peptide that includes a sequence of consecutive amino acids found within amino acids 695 to 699 (SEQ ID NO. 11) of the human blood clotting factor Va.

88. The method of claim 87 wherein the effective amount of the peptide is in the range of from about 0.01 to 1000 mg/kg of body weight, per day.

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89. The method of claim 88 wherein the effective amount of the peptide is in the range of from about 0.1 to 100 mg/kg of body weight, per day.

5 90. The method of claim 89 wherein the effective amount of the peptide is in the range of from about 1 to 10 mg/kg, of body weight, per day.

91. A method for inhibiting thrombin generation in a human patient suffering from a blood coagulation disorder, the method comprising:  
10 administering to the patient an effective amount of a peptide analogue that mimics the peptide of the method of claim 87.

92. A method for inhibiting thrombin generation in a patient suffering from a blood coagulation disorder, the method comprising:  
15 administering to the patient an effective amount of a peptide that includes an amino acid sequence DYDY (SEQ ID NO. 10).

93. The method of claim 92 wherein one of the Y amino acids of the amino acid sequence is sulfonated.  
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94. The method of claim 93 wherein the amino acid sequence is DY(-SO<sub>3</sub>)DY.

95. The method of claim 93 wherein the amino acid sequence is  
25 DYDY(-SO<sub>3</sub>).

96. The method of claim 92 wherein both of the Y amino acids of the amino acid sequence are sulfonated.

30 97. The method of claim 96 wherein the amino acid sequence is DY(-SO<sub>3</sub>)DY(-SO<sub>3</sub>).

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98. The method of claim 92 wherein the effective amount of the peptide is in the range of from about 0.01 to 1000 mg/kg of body weight, per day.

5 99. The method of claim 98 wherein the effective amount of the peptide is in the range of from about 0.1 to 100 mg/kg of body weight, per day.

10 100. The method of claim 99 wherein the effective amount of the peptide is in the range of from about 1 to 10 mg/kg of body weight, per day.

101. A method for inhibiting thrombin generation in a patient suffering from a blood coagulation disorder, the method comprising:  
administering to the patient an effective amount of a peptide  
15 analogue that mimics the peptide of the method of claim 92.

102. A method for inhibiting thrombin generation in a patient suffering from a blood coagulation disorder, the method comprising:  
administering to the patient an effective amount of a peptide that  
20 includes an amino acid sequence DYDYQ (SEQ ID NO. 11).

103. The method of claim 102 wherein one of the Y amino acids of the amino acid sequence is sulfonated.

25 104. The method of claim 103 wherein the amino acid sequence is DY(-SO<sub>3</sub>)DYQ.

105. The method of claim 103 wherein the amino acid sequence is DYDY(-SO<sub>3</sub>)Q.

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106. The method of claim 102 wherein both of the Y amino acids of the amino acid sequence are sulfonated.

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107. The method of claim 106 wherein the amino acid sequence is DY(-SO<sub>3</sub>)DY(-SO<sub>3</sub>)Q.

108. The method of claim 102 wherein the effective amount of the peptide is in the range of from about 0.01 to 1000 mg/kg of body weight, per day.

109. The method of claim 108 wherein the effective amount of the peptide is in the range of from about 0.1 to 100 mg/kg of body weight, per day.

110. The method of claim 109 wherein the effective amount of the peptide is in the range of from about 1 to 10 mg/kg of body weight, per day.

111. A method for inhibiting thrombin generation in a patient suffering from a blood coagulation disorder, the method comprising:  
administering to the patient an effective amount of a peptide that mimics the peptide of the method of claim 102.

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